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DISEASES OF THE NERVOUS SYSTEM

A PRACTICAL JOURNAL ON PSYCHIATRY AND NEUROLOGY

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DISEASES of the NERVOUS SYSTEM

A PRACTICAL JOURNAL ON PSYCHIATRY AND NEUROLOGY

Nicotinic Acid Therapy and the Chronic Schizophrenic

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North Battleford, Saskatchewan

(A Pilot Study)

Introduction

Throughout the world today medical research in the psychiatric field centers upon unravelling the enigma of schizophrenia. The inadequacy of current physical treatments to meet the problem necessitates a continuous search for better means of combating and treating this mental illness. Too often our new understanding and approach are reserved for early schizophrenics for whom a good prognosis is more probable while in the back wards of our hospitals sit the chronic, regressed schizophrenics, neglected, lost in a world of phantasy, often impulsive and aggressive, grim reminders of our past failures. In many hospitals the treatment of chronic, regressed schizophrenics can be little more than custodial care. Only through investigating the effects of various untested treatments will our understanding of these patients broaden and their numbers diminish. The use of Nicotinic Acid has been proposed as a new treatment of schizophrenia. The purpose of this paper is to set forth the results of the application of this drug to chronic schizophrenics housed in a "back" mental hospital ward.

I. PREAMBLE.

Lehman's[1] "Niacin Therapy in Psychotic States" found in "The Biology of Mental Health and Disease" covers the field very adequately. Other work in the field has been carried out mainly with presenile and senile groups of patients. Gregory,[2] using 300 milligrams of Nicotinic Acid three times a day orally and 160 milligrams parenterally, found it useful in the treatment of seniles.

Noted improvement in patients was found by Moore[3] using a combination of Histamine and Nicotinic Acid combined with "total push" therapy in the treatment of psychosis with cerebral arteriosclerosis. Levy,[4] using an elixir containing perdrachm, three grains of pentylenetetrazol and 100 mg. Nicotinic Acid with compound pepsin elixir, found this combination effective in the treatment of the aged, especially those with only mild memory defects, confusion and deterioration, and no more serious emotional and psychotic disturbances.

The usefulness of Nicotinic Acid in the treatment of delirium tremens has been known for years. Mainzer and Krause[5] believe that lack of this vitamin is an important factor in the development of delirium tremens.

Thompson and Proctor[10] have carried out an experimental study of the effects of Nicotinic Acid and Phenobarbital on depressive and anxiety reactions. The results obtained by them were, a definite improvement in 34% and some improvement in 47.2% of patients reported. Recent experimentation with Nicotinic Acid on acute schizophrenics by Hoffer et al.[6] stimulated the running of a pilot project with chronic schizophrenics using the dosage suggested by the results of the original study. Following the results achieved by the writer[7] with occupational therapy and refractory patients, it was felt that perhaps

Nicotinic Acid might be beneficial in treatment of the chronic regressed, deteriorated schizophrenics.

(2) *Properties of Nicotinic Acid.*

1. It is a pyridine derivative and is thermostable. A component of the pyridine nucleotides, it is concerned in a co-enzyme system which plays an important role in the hydrogen transporters of cellular metabolism. An indispensable factor of cellular metabolism, these co-enzymes for dehydrogenases are links in the chain from metabolite to final oxidation by cytochrome oxidase.[1]

2. A peripheral dilator.

3. Regarding cerebral circulation, a difference of opinion exists at the present time. Aring et al.[12] claims an increase of 20% following the taking of Nicotinic Acid in the blood flow. Schernberg[13] came to the conclusion that no increase occurred.

4. Himwick[11] has explained in detail the role of Nicotinic Acid in carbohydrate metabolism and cellular respiration.

(3) *Mechanism of Action.*

1. Lehman[1] feels Nicotinic Acid produces its effects by saturation which may shift the balance of the co-enzyme systems involved in cellular metabolism to produce a new compensatory mechanism.

2. Hoffer et al.[1] postulate three possible functions of Nicotinic Acid.

a. To restore inhibited DPN-TPN function.

b. To inhibit methylation of NOR adrenalin to adrenalin.

c. To inhibit sympathetic response to parasympathetic stimulation.

They are of the opinion that the first function appears most likely.

II. STRUCTURE OF THE PROJECT.

(1) It was decided to select eleven of the most refractory, regressed, deteriorated female patients who had derived no benefit from the various forms of treatment available, including lobotomy, insulin, E.C.T., occupational therapy and psychotherapy, whose behavior was such that they represented a nursing problem, and who had been ill a number of years. Their physical and mental condition, which has been static for a number of years before the onset of the treatment, is to be compared before and after treatment.

It is proposed to give two short case histories as an illustration of the type of cases.

TABLE I

Composition of Treated Group

Patient	Age	Diagnosis	Length of Stay in Hospital Years	Previous Treatment
1	46	Schiz Cat	19	Lobotomy, E.C.T.
2	35	Schiz Heb	15	Hydrotherapy, E.C.T.
3	32	Schiz Cat	15	E.C.T., Insulin Lobotomy
4	26	Schiz Cat	3	E.C.T., Insulin, Lobotomy
5	49	Schiz Heb	17	E.C.T., Insulin
6	38	Schiz Heb	21	Hydrotherapy, E.C.T.
7	34	Schiz Heb	15	E.C.T., Hormone Therapy, Lobotomy
8	48	Schiz Heb	22	E.C.T., Hydrotherapy
9	48	Schiz Cat	20	E.C.T., Hydrotherapy
10	45	Schiz Heb	11	E.C.T., Hydrotherapy
11	50	Schiz Heb	20	E.C.T., Insulin, Lobotomy

Occupational Therapy and Recreational Therapy were tried with all the above patients in order to try and rehabilitate them. Sedation used in all cases in order to control their aggressive outbursts.

These treatments had no effect either on the behavior or mental condition of the patients.

(2) *Methods to evaluate.*

a. Mental status before and after trial period.

TABLE II

Composition of Control Group

UNNTREATED SCHIZOPHRENICS—FEMALES

No. of patients	Diagnosis	Age Range	Length of stay in hospital range	Previous treatment
29	Schiz Hebephrenia	38-58 years	3-29 years	29 had E.C.T. 14 had Lobotomy 9 had Insulin Coma 12 had Hydrotherapy
14	Schiz Catatonia	21-59 years	3-29 years	14 had E.C.T. 5 had Lobotomy 6 had Insulin Coma 5 had Hydrotherapy

b. Ward behavior report by the ward supervisor before treatment, weekly, during treatment and after treatment.
c. Gardiner behavior charts weekly.
d. Seclusion record.
e. Accident record.
f. Statistical evaluation of results whenever possible.
g. Control group of 43 untreated chronic schizophrenics.

Occupational Therapy and Recreational Therapy were tried with all the above patients in order to try and rehabilitate them. Sedation was used to control their aggressive outbursts.

This group was selected on account of their similarity to the treated group in the following categories:

(1) Diagnosis
(2) Mental Status
(3) Length of stay in hospital
(4) Non-response to all forms of treatment
(5) Seclusion record

(3) *Dosage.*

Dosage is to consist of 1 gram of Nicotinic Acid orally t.i.d. with the trial period to consist of 8 weeks. This dosage of 3 grams a day was found effective in the treatment of acute schizophrenics by Hoffer et al.[6] and this was used as a guide to the dosage in this trial. Difficulty was found in getting the patients to take their capsules in view of their mental condition and also in view of the unpleasant taste. This was overcome by mixing the powder with glucose flavored with orange.

Illustrative Cases

1. *Mrs. M. S.*

A catatonic schizophrenic, aged 46 years, was admitted to this hospital on February 12, 1935. On admission she was mute, resistive and negativistic. Periodically aggressive, she was continually disrobing and wrapping her head in sheets. Despite a variety of physical treatments she became increasingly filthy in her habits and more violent in her outbursts. She became a violent and aggressive patient on whom E.C.T. and sedation had no effect. As the years went by her habits deteriorated, any slight interest in her surroundings diminished and she became completely unsocialized and uncontrollable. In view of this the patient was placed in continuous seclusion. On January 9, 1953 a lobotomy was performed in an attempt to resocialize the patient. Following the lobotomy the following was the picture of the patient:

She has been secluded because she attacks the other patients without provocation, has frequent outbursts of violence during which she throws everything that she can get a hold of. After many attempts of resocialization patient had to be returned to continuous seclusion.

Mental Status Before Nicotinic Acid.

Patient is in permanent seclusion. She is destructive, filthy and self abusive. Inaccessible to mental examination, she lies in bed in her room giggling to herself. Becomes exceedingly violent and excited when anybody is cleaning in the vicinity of her room. E.C.T. and sedation have no effect in controlling the patient.

2. *Miss B. W.*

A schizophrenic, hebephrenic type, 35 years old, single woman was admitted to this hospital on June 4, 1939. On admission there was noted disharmony of mood and thought, silly fatuous laughter, ideas of persecution, apathy and withdrawal. She displayed no interest in her surroundings. Despite the various physical treatments, including hydrotherapy and numerous extended courses of E.C.T. on a symptomatic basis, the patient's condition steadily deteriorated. She became very impulsive, destructive and filthy in habits. Mute at mental examination, apparently actively hallucinating, she sits laughing to herself and resists any attempt at socialization.

Mental Status Before Nicotinic Acid.

Patient was inaccessible to mental examination. Destructive with periods of violence during which she breaks many windows, her habits are filthy and she is irrational in behavior. She displays homosexual tendencies and is continually destroying her clothes. The patient is pale, emaciated and her appetite poor.

TABLE III

Gardiner Behavior Chart

	Monthly Before Treatment				Weekly On Treatment							
Appearance	0	1	0	0	0	0	0	0	0	0	0	0
Sleep	2	3	2	2	2	2	3	3	3	3	2	3
Appetite	2	2	2	2	2	2	2	2	2	2	2	2
Sociability	0	0	0	0	0	0	0	0	0	0	0	1
Activity Control	0	0	0	0	0	0	0	0	0	2	2	2
Noise Control	2	2	0	0	0	0	0	0	0	2	2	3
Temper Control	0	0	0	0	0	0	0	0	0	0	1	3
Combativeness Contr.	0	0	0	0	0	0	0	0	0	2	2	3
Care of Property	0	0	0	0	0	0	0	0	0	1	1	2
Self Entertainment	0	0	0	0	0	0	0	0	0	0	0	1
Coop. in Routine	0	0	0	0	0	0	0	0	0	1	1	2
Work Capacity	0	0	0	0	0	0	0	0	0	0	0	0
Intiative, Alone	0	0	0	0	0	0	0	0	0	0	0	0
Initiative, Supervised	0	0	0	0	0	0	0	0	0	0	0	0
Directability	0	0	0	0	0	0	0	0	0	0	0	0
Rating	6	8	4	4	4	4	5	5	5	13	13	22

The above chart is the record of the patient B.W. reported in this paper.

For one year prior to the advent of this study, the above chart was used as a guide to the condition of each individual patient on the ward.

Prior to this study the patients were rated by the ward supervisor and her relief on a monthly basis. In this way it was felt that the raters had adequate experience in rating.

In this study the rating was carried out on a weekly basis by the ward supervisor and her relief. Throughout the project the same two people were involved. It is also to be noted that the rating on these patients for the 6 months prior to the treatment was carried out by the same two nurses.

The rating consisted of the observations of (1) the ward supervisor (2) on a consultative basis between the ward supervisor and the nurses who had daily contact with patients, each patient being dealt with individually. Each rating was based on a week's observation of the patient and took at an average of 15 minutes to score. A key to the rating was supplied to the ward supervisor. The following is an example of how the rating was carried out.

Noise Control

0—None—Mentally disturbed, noisy most of the time, shouting, etc.

1—Poor—Rather noisy at times or a little noisy all the time.

2—Fair—Quiet most of the time but moderately noisy occasionally or frequent low mutterings.

3—Good—Never causes noisy disturbance.

4—Extra Good—Very quiet.

TABLE IV

Gardiner Behavior Charts

TREATED PATIENTS

Name	Mean Rating achieved for the 6 months prior to treatment	Rating at the start of treatment	Rating after 8 weeks of Nicotinic Acid
M.S.	9.16	10	28
R.F.	17.00	7	31
S.O.	19.00	18	26
D.N.	10.17	9	11
M.H.	5.83	3	14
R.H.	13.17	11	18
B.W.	5.67	4	22
W.B.	27.67	29	32
M.B.	12.67	9	20
J.R.	22.00	22	23
F.T.	11.83	12	37
Mean	14.02		23.82
Standard Deviation	6.51		7.55

Applying null hypothesis to the above means the critical ratio (difference between means/standard error of the difference) was found to be 4.17. For ten degrees of freedom at the 1% level of significance the ratio is 3.17. The null hypothesis was therefore refuted.

Difference Between Means Very Significant at 1% Level

In a breakdown of the figures of the Behavior Charts, we find the following factors:

1. Sleep improved in all patients.
2. Appetite increased in all patients.
3. Directability better in 6 patients.
4. Temper control and combativeness control better in five patients.
5. Initiative alone better in 4 patients.
6. Co-operation in routine better in 4 patients.
7. Care of property better in 3 patients.

Control Group:

Statistically the figures were not significant.

Accident Record:

Incidents were not significantly altered in either the treated or control group.

TABLE V

Comparison of Hours of Seclusion

	Two-Month Period Prior to Treatment		*Two-Month Treatment Period*		
	No. hours seclusion	Mean no. hours seclusion	No. hours seclusion	Mean no. hours seclusion	Percentage Reduction
Treated Group N=11	3423	311.18	330.75	30.07	90.34
Untreated Group N=43	2947.25	68.54	376	18.74	88.72

Percentage reduction due to change in nursing approach=88.72.

Therefore percentage reduction due to therapy=1.62.

The whole project resulted in better psychiatric care and attention to all patients on the ward. Before the project started the nurses were orientated towards a better understanding of the needs and care of chronic mentally disturbed patients. This fact explains the considerable reduction of hours of seclusion in the untreated group which consisted of chronic schizophrenics. Over and above this the treated group showed a greater reduction of seclusion hours.

IV. CONCLUSIONS.

Three patients showed improvement and it is proposed to illustrate this by the findings after the trial on the two patients already described earlier in this paper.

M. S. Patient's appearance improved slightly, she likes to be dressed and is now amenable to toilet training, sleeping better, her appetite is good and she goes to the cafeteria where she now eats with a spoon. She plays games but these are restricted as she sometimes becomes upset. Attending picture shows, church and going for walks now, she is only noisy when she is upset by other patients. More amenable to nursing care and direction, she now looks at books, sews and makes clothing for a doll she has adopted. She will engage in domestic activities. According to the nurses who speak her language her conversation is at times quite rational. She came to interview quite readily and chattered away in her own language. Her delusions, hallucinations and disharmony of mood and thought are still present. She smiles fatuously when she is asked a question. Seclusion has been markedly cut down.

B. W. Her appearance is slightly improved, she is now amenable to toilet training. Sleeping and eating better, she has gained weight. She is, however, usually seclusive and is reluctant to join in ward activities. No longer restless (previously was breaking windows, etc.), she has not been secluded for some time. Idle usually, she does minor damage occasionally to clothes, tearing buttons off, etc. Her homosexual activities have completely stopped. Conversing in an infantile manner occasionally, she has started eating in the cafeteria. In the interview situation, the patient attempted to answer questions but her answers were irrational, she was withdrawn and showed marked disharmony in mood and thought and retained her delusional system.

In the three improved patients the following are the findings:

1. Seclusion has been greatly reduced.
2. Noise and temper tantrums, combative trends redirected. They can usually be handled by the nursing staff.
3. Their violent and aggressive outbursts are much less.
4. Homosexual activities have stopped.
5. They are more amenable to ward routine.
6. Will move according to the group.
7. Appetite and weight improved.
8. Their habits are much better than before.
9. They retain their delusions, hallucinations and other schizophrenic features.

In the other eight patients on the project no marked change was noted. Generally, appetite was increased and outbursts of violence and aggression were slightly decreased which is probably due to better handling by the nursing staff. This factor should also be considered in the improved group.

SUMMARY.

Nicotinic Acid 1 gram t.i.d. was given orally to 11 chronic, regressed, deteriorated schizophrenics for an 8 week trial period. Three of the patients showed an improvement as estimated by their behavior. No

change was noted in their delusions, hallucinations and other schizophrenic features. Eight patients showed a slight improvement which is primarily attributed to better nursing care and attention. While this trial does not show Nicotinic Acid to have any effect on the schizophrenic process per se, it is felt that Nicotinic Acid should be further investigated in a larger trial series. Lucy[9] found chronic schizophrenics to have a greater tolerance to histamine than in acute cases, so comparatively speaking perhaps the dosage of Nicotinic Acid used in this trial was inadequate.

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Modified Electro-Convulsive Therapy With Unidirectional Current

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Until recently only the Cerletti-Bini method of electrical stimulation was used to produce a convulsion at Rockland State Hospital. Although it produces very favorable results in certain psychiatric conditions, this method also produces complications which Impastato divides into three groups:

1. Somatic (fractures, dislocations)
2. Physiological (apnea)
3. Mental (confusion, memory impairment, post convulsive restlessness)

Occasionally there are respiratory and circulatory side effects—some even fatal.

The danger of somatic complications was recognized a long time ago. Bennett, in 1940, reported the use of curare for the prevention of fractures in E. C. T. Since then magnesium sulfate, quinine metachloride, sodium amytal, glucose, dilantin, bromides, calcium, and recently flaxedil and succinyl chloride have been used as muscle relaxant drugs.

Friedman, Wilcox and Reiter believe that side effects are due to the fact that massive alternating currents are used in E. C. T. They suggested the use of unidirectional current,

From Rockland State Hospital.

of longer duration but of far less amperage.

The writer introduced this type of modified electrotherapy at Rockland State Hospital and this is a report on its use for a period from January 1954 to December 1954.

Patients recommended for electrotherapy were divided at random into two groups. One group, consisting of 170 patients (see table), was treated with unidirectional current; the other group, consisting of 360 patients, was treated with the standard alternating current method and served as controls. The combined convulsive non-convulsive method was used. This method was first described by Leo Alexander of Boston.

Technique

Patients are prepared in the usual way, and treatment given in the morning before breakfast. Special electrodes are used which have been immersed in a very weak saline solution. No mouth protection is needed since the tongue does not protrude as in the C-B method, and there is no danger of biting the tongue. No jelly is used and no pillow is placed under the spine. One attendant guards the patient's shoulders, patient's hands are folded on the chest, and the lower extremities are not protected. Frontal application of the electrodes is used. The latter may be applied before the treatment, or they may be held in place by an assistant while the treatment is given. Reiter's machine, Model CW47C, which delivers a spiked unidirectional current, is used.

The current selector knob is turned to position "3" and a current of 10 milliamperes is applied. Current of this intensity usually renders the patient unconscious instantly, which is an important factor when no anaesthesia is used. To be safe, however, the current is raised rapidly until the tonic phase commences. If a lower current is used, it may be felt by the patient. This is unpleasant and painful. As soon as the patient is in the tonic phase, current is reduced to 5-7 milliamperes and kept at this level during the entire period of treatment. In this way, the clonic phase is suppressed and convulsions are much milder. If the current is decreased further during the clonic stage, convulsions become more pronounced.

At the end of the clonic phase (which is noted by increased intervals between contractions) the current is changed to non-convulsive (current selector knob is turned to position "1") and current is given for another ½-1 minute (½-1 milliamperes). This current stimulates the respiratory center and the patient resumes breathing immediately after the convulsion is over. If there is any difficulty in breathing, which occurs rarely, stimulation of the respiratory center is achieved by a burst of current, raising to about 5 milliamperes and decreasing to 1 milliampere.

The recovery stage is shorter than with the standard method; there are fewer headaches and no memory disorders nor confusional states. Patients are usually up and able to respond with clear minds within one to five minutes; and are accessible to psychotherapy shortly after E. C. T. with complete amnesia for the latter.

Confusional states and temporary memory impairment were considered by earlier schools as part of the treatment and as a necessary step in the patient's improvement. It is now recognized that these are complications and side effects rather than part of the treatment.

From our experience, gained during almost one year of UDC administration, we have reached the following conclusions as to the difference between the UDC and C-B methods:

In the C-B method, the patient gets all the electrical current in a split second (0.1-0.5 second). With the UDC method, the patient is under electrical current during the entire treatment period. However, much less amperage is used than in the C-B method.

In humans, when electrically induced convulsions are produced with a convulsive dose of alternating current, the tonic phase lasts about ten seconds and the clonic phase about thirty five seconds. The period preceding the tonic phase is about two seconds. Leo Alexander calls this stage the "Period of latency." This phase may not necessarily be followed by a convulsion, depending upon whether or not the stimulus was at or above the convulsive threshold.

When UDC is applied to produce a convulsion, the period of latency lasts about ten seconds, the tonic phase about thirty-five sec-

onds and the clonic phase about ten seconds. By continuous stimulation, the clonic phase can be eliminated if the current is kept at 5-7 milliamperes during the entire period. However, if the current is further reduced, only partial suppression of the clonic phase will take place. The more the current is reduced during the clonic phase, the more pronounced are the clonic movements. If complete suppression of this phase is achieved, patient remains in a tonic state throughout the entire treatment period.

In the C-B method, the apnea routinely persists longer than the convulsion, and sometimes leads to serious complications. Some therapists even use artificial respiration after each treatment for the prevention of apnea. When UDC is used and the clonic phase is suppressed, the patient usually resumes breathing immediately after the convulsion is over, and as noted before, if there is a slight respiratory delay, which seldom occurs, patient is stimulated by short bursts of current, raising to about 5 milliamperes and decreasing to 1 milliampere. In general, it can be stated that in all our cases so treated, there was not a single case of respiratory embarrassment.

With the UDC method there is no opening of the mouth at the beginning of the treatment as in the C-B method, therefore no danger of dislocation of the jaw. No mouth piece is used because there is no protrusion of the tongue, therefore no danger of biting the tongue. No patient has bitten his tongue in all treatments performed with this current. Epileptic cry and conjugate deviation of the eyes and head to one side are also eliminated.

The handling of patients who are resistant to treatment is always a difficult problem. In the C-B method, the patient must be recumbent before treatment can be administered. It is usually necessary for several attendants to assist with the treatment and the application of strong manual "protection" may be the cause of complications. Administration of barbiturates does not solve the problem because of the need for several attendants to assist in giving the struggling patient the injection. Moreover, barbiturates increase the incidence of respiratory complications and it becomes necessary to increase the electrical dose to produce a convulsion.

With the UDC method, if the patient is resistive to treatment, charged electrodes may be applied to his forehead regardless of his position—even sitting. At the same time, the assistants are enabled to place the patient in a suitable position for treatment. No complications were experienced in handling a considerable number of very disturbed patients.

The percentage of fractures due to treatment has been greatly reduced since metrazol was replaced by electric current. But fractures continued to be the most frequent complication to E. C. T. The glissando attachment did not decrease the number of fractures. The percentage of fractures has been rather stable at Rockland State Hospital for the past several years. While treating 170 patients with UDC there was one bony complication: a fracture of D5 in a 35-year-old female. For the same period there were nine fractures of the spine while treating 360 patients with the standard method.

This is in line with the investigations of Impastato and Wilcox using the UDC.

The use of muscle relaxant drugs has been eliminated since the introduction of UDC at Rockland State Hospital. In all cases where because of special indication, as bony or cardiac pathology, mild muscle contractions are required, modified E. C. T. is given. Where previously muscle relaxant drugs were used, treatment is now given with UDC, but the current is increased gradually, beginning at zero milliamperes until the patient enters into a tonic phase.

As an anaesthetic, 5% sodium pentothal or surital is used. Before the initial treatment, each patient is tested, the amount of barbiturates required to produce complete anaesthesia is established and a like dose is usually given in all subsequent treatments. This test was described by Dr. David Impastato.

Two electrodes are placed over the temples and the current selector knob is turned to position "1." 5% of sodium pentothal or surital is administered intravenously and injected at the rate of 3 cc per minute. Patient is asked to count and the drug is introduced until speech becomes slurred. Injec-

tion is then stopped and ½ minute is allowed to elapse for the drug to develop its action. Current is then turned on, beginning at zero, is slowly advanced, and the patient is observed for signs of pain. If this occurs before the meter registers 2½ milliamperes, the current is turned off, an additional cc. of sodium pentothal is injected and the procedure is repeated. Patient should be able to tolerate 2½ milliamperes without pain, after which he should be able to receive ten or more milliamperes without discomfort.

The convulsion is milder and there is no danger of complications such as sometimes occur after barbiturate administration. If side effects of barbiturates are noted, the most effective corrective is the application of UDC, after which the side reactions disappear.

Twelve patients, who ordinarily would have muscle relaxant drugs administered, received this modified type of E. C. T. Seven were suffering from spine pathology, four from heart pathology, and one had a fracture of the pelvis. No ill effects were observed after this type of treatment.

Less help is necessary when administering treatment with the UDC method. Instead of at least two attendants, as in the C-B method, only one attendant is needed to guard the shoulders while the physician applies the current. With the constant shortage of help in state hospitals this factor is of major importance.

After treatment with UDC there are fewer headaches, less retrograde amnesia, and little or no memory impairment. Patient is reoriented much faster and has less aversion to treatment.

In the C-B method, there are occasional complications due to the patient's inhalation of saliva, which is produced excessively during the treatment. This complication may occur even if the patient is turned on his side immediately after the convulsion is over. Lung abscesses have been described as a complication. There is no danger of inhaling saliva with the UDC method because the saliva flows from the mouth during the treatment.

This method of treatment causes less strain on the heart muscle than the C-B method. When treatment is given with the conventional machine, the following events usually take place during the convulsion:

1. The muscles contract.
2. The arterial vessels constrict.
3. There is increased peripheral resistance.
4. Valsalva phenomenon occurs.

With the first breath after apnea, the venous blood rushes to the heart and at the same time peripheral resistance is increased. Therefore the heart has to master severe strain with danger of myocardial damage, or of some complication if it is a diseased heart, especially when combined with post-shock apnea. When UDC is given and the clonic phase is suppressed by continuous stimulation, the muscle contractions are milder, the Valsalva phenomenon is gradually relieved and the sudden rush of venous blood to the heart, after the clonic phase, is prevented. Peripheral vaso-constriction is also eliminated and there is no apnea. Patients with heart pathology therefore may be treated with greater safety.

Comparing the clinical results of the group treated with UDC and the standard method, the difference is insignificant. The percentage of improved patients and the number of treatments necessary in both groups was about the same.

Some critics state that with the UDC method they are never certain that the patient has a real convulsion, that the brain is irritated by the current, and that although the patients perform some movements it is doubted that they achieve a convulsion—a condition required for the patient's improvement.

There is a simple method to determine whether or not the patient experiences a real convulsion. By decreasing the current to low amperage (1-2 milliamperes), if he has a real convulsion, patient will continue to convulse after the current is reduced. A real convulsion, once started, continues with no current. If it is not a real convulsion, involuntary movements disappear.

Summary and Conclusions

The use of electro-convulsive therapy with unidirectional current on 170 patients in a state hospital has been described. The convulsive—non-convulsive method was administered. This type of treatment was com-

pared with the standard Cerletti-Bini method. When properly applied, the amount of current is individualized and the patient receives only as much as is required to produce a convulsion. The latter is milder, and the clonic phase may be suppressed by continued stimulation so that only the tonic type of convulsion is induced.

Although the patient is under electrical current for the entire period of treatment, less amperage is used. As a result, little or no confusion and memory impairment, as side effects of the treatment, are observed. Patients respond with clear minds shortly after treatment and are accessible for psychotherapy. Somatic complications are greatly reduced and there is no apnea.

The unidirectional current type of treatment causes less strain on heart muscle and patients with diseased hearts may be more safely treated. The danger of inhaling saliva and the accompanying pulmonary complications, which may sometimes occur with the C-B method, are eliminated with UDC. Muscle relaxant drugs may be replaced by this type of modified therapy and use of barbiturates. Complete anaesthesia is obtained with a minimal amount of barbiturates according to the test described above, and there is no danger of side effects of barbiturates.

The clinical results and the number of treatments necessary to produce a remission are the same with this method as compared with the Cerletti-Bini method.

TABLE I

Diagnosis and Clinical Results of Patients Treated With Combined Convulsive- Non-Convulsive Method.

	Unimproved	Improved	Much Improved and Recovered	Total
D. P. M.	10	30	5	45
D. P. C.	9	28	12	49
D. P. P.	9	15	9	33
Childhood Schizophrenia	6	2	1	9
M. D. M.		2		2
M. D. D.		2		2
Involutional Psychosis — Mixed			2	2
Involutional Psychosis Mel.	1	11	6	18
Involutional Psychosis Par.	2	3	4	9
Psychoneurosis Mixed		1		1
Totals	37	94	39	170

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Tension Headaches and Their Treatment

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Since headaches may be due to many different factors, it often entails considerable detective work on the part of the physician to find the precipitating factor and underlying cause. If the etiology of the headache can be attributed to a brain tumor, sinusitis, neuralgia, uremic poisoning, cerebral vascular accidents, alcohol, or other toxic products, then the successful removal of these underlying conditions usually means the end of the headaches.

The actual cause of tension headaches is unknown. Several investigators, notably Wolff,[1] have postulated that emotional tension may cause a change in the caliber of certain cranial arteries. Another contributing factor to tension headaches is the presence of contraction or tension of the muscles of the head and neck.[2] In a study of 400 tension headaches, Friedman et al[3] concluded that tension headache is an emotionally induced physiological reaction to various situations productive of anxiety. Three quarters of their patients were aware of emotional difficulties as a precipitating cause of the headaches. Many patients in this study had tension headaches beginning early in life. The most frequently observed emotional conflicts in these patients were aggression, hostility, and intense resentment against members of their family or persons who represented family figures (identification).

Tension headaches are undoubtedly the most common types of head discomfort encountered by the physician. It frequently has been confused with migraine, but careful study will reveal that the tension headaches are quite different. The tension headache patients frequently have the same sensitive, tense, emotionally unstable makeup as the migraine patients. However, as Marcussen and Wolff[4] have pointed out, they are not necessarily neurotic and may have made a very successful adjustment in life. They are, however, usually tense, rigid, and ambitious perfectionists who because of their inner feelings of insecurity often succeed only at the expense of greater effort with the resultant nervous tension to their brain or body as a whole.

The tension headaches usually differ from migraine in the following respects:[5] 1. There are no prodroma symptoms such as visual scotomata or nausea. 2. The head pain is usually described as vague, dull, bilateral, or often as sensations of pressure in the head which may be accompanied by muscular tension and spasms in the neck or scalp muscles. 3. Frequently nervous tension cephalalgia follows or comes on concurrently with periods of emotional stress. In women tension headaches seem to be frequently associated with menstrual periods. The emotional conflicts precipitating tension headaches may be unconscious. The bringing to light or an adequate resolution of these conflicts often results in an end to the headaches.

Since emotional difficulties are the basis for nearly all tension headaches, the prevention of future attacks is one of adequate analysis of the emotional problems and sufficient psychotherapy to effect relaxation or adequate adjustment of the individual to his environment. Obviously the complete avoidance or removal of all nervous tension in anyone is virtually impossible. We have to live, work, and play in an era which is characterized by speed, competition, high cost of living, threat of war and frustrations. The emphasis in psychiatric treatment in the past decade has been to try to effect a control of emotional conflicts through brief supportive or symptomatic therapy rather than through more expensive and time consuming intensive psychoanalysis. Thus, there has been a concerted effort to treat various types of nervous conditions with medical or physical agents.

Analgesic properties of acetylsalicylic acid and acetophenetidin have been known and made use of for many years in treating headaches and various muscular discomforts. The use of caffeine for headaches has been used

more recently on the basis that it is a central nervous stimulant, reducing fatigue and when taken orally is thought to act as a vasoconstricting drug. A mild sedative has often been used in conjunction with analgesics for headaches to reduce nervous tension.

A new preparation for treating nervous tension headaches has been introduced to the physician within the past two years.[6] This agent is known as Fiorinal and is a tablet compounded of 50 mgm. of Sandoptal (isobutylallylbarbituric acid), 200 mgm. of acetylsalicylic acid, 130 mgm. of acetophenetidin and 40 mgm. of caffeine. Sandoptal is a mild sedative, possesses a wide margin of safety and is well tolerated. It has been found to augment the action of analgesics for the relief of pain, especially that of the neuralgic type. The main difference between Fiorinal and other headache drugs is that the sedative, Sandoptal, has been added and the caffeine has been retained. A mild sedative as that used in Fiorinal tends to decrease the hyperirritability which is so often present in tension headaches.

In order to test the efficiency of Fiorinal, fifty patients who had symptoms suggesting nervous tension cephalalgia were selected at random. Several patients in this series had old cerebral concussions, hypertension, or atypical migraine attacks. Many had been treated for psychoneurosis, reactive or involutional depressions, and a few for manic-depressive or schizophrenic psychoses. There were thirty-five men and fifteen women included in this study. The ages of the patients ranged from eighteen to seventy-two years of age. The average length of follow-up of the patients in this series was about eight months with an average visit of every three weeks. A few patients were seen only two or three times and either chose not to return to this office or went elsewhere for treatment. This, of course, cannot be easily avoided in a private practice since treatment of patients is entirely on a voluntary basis.

The average dose of Fiorinal was one tablet every four hours beginning at the onset of their headaches. Most of the patients were instructed not to exceed four to six tablets daily and to avoid taking any other strong sedative preparations with the Fiorinal. In the majority of patients, the sedative effect of this preparation appeared to be very slight or nonexistent. Some patients began with two tablets at the onset of the headache. The majority of the patients obtaining relief with Fiorinal reported that it took about thirty minutes for the desired relief of the headache to take place. In more protracted cases relief was not obtained until the second or third dose of the preparation was taken.

A specially prepared headache chart was made out for each patient. This served as a rather complete record of the family history, known contributing causes, prodromata, localization of the head pain, description of the head pain, occurrence, duration, severity, frequency, course of the headache, associated manifestations during the headache, extent the headache was incapacitating, migraine equivalents, x-ray studies, neurological examinations, EEG, previous treatment and results, present diagnosis, psychotherapy, interval of treatments, and results.

The results were classified as good, fair, or poor relief of the headaches. Twenty-four, or 48 per cent of the patients stated that they had good relief from their headaches while taking Fiorinal. Twenty patients, or 40 per cent said that they had only fair improvement in their headaches. No relief from headaches was present in six patients, or 12 per cent. Nineteen of the twenty-four patients who were relieved by this drug appeared to have fairly typical nervous tension headaches. Five patients who claimed rather good relief from the use of Fiorinal showed that two had atypical migraine attacks, one had hypertensive headaches, and two patients had had head injuries but not of recent origin.

Of the failures reported for relief of headache with Fiorinal, three had tension headaches and three had atypical migraine attacks. It is interesting to note that six cases with postconcussion syndromes all stated that they had fair relief of their headaches with this drug.

It was also noted during this study that several patients who had acute upper respiratory infections or possible sinus infections also benefited from the use of Fiorinal.

This fact was also noted in the studies made by Ryan.[7]

In analyzing the data from the headache charts, it was noted that a family history of headaches or migraine was present in about 22 per cent of the patients. Emotional factors appeared to be a contributing cause in over 90 per cent of the patients examined for headaches in this study. Physical fatigue was a very definite and important accompanying symptom along with emotional factors. Excessive use of alcohol or tobacco seemed to be a contributing cause in about 50 per cent of the severe headache cases. No specific relationship to changes in weather, food allergies, or changes in posture appeared to be significant in this study. However, menstruation appeared to be a contributing cause for so-called tension headaches in the majority of women who were in the age group of patients who menstruated. No specific prodroma symptoms appeared to be consistent in the tension type of headaches. Occasionally patients felt nauseated, but rarely was there the severity of nausea and vomiting as seen in the typical migraine headache attack. The two most common locations of tension headache appeared to be either frontal or occipital. In about a quarter of the cases, patients complained of generalized headaches or a generalized soreness or pressure feeling on the top or around the head.

Descriptions of the type of pain and the duration and severity were extremely variable in the so-called tension headaches. The majority of the patients, however, stated that the head pain was usually constant, occurred usually towards the end of the week or after an unusually busy or trying day at work. Rarely did patients complain that their tension headaches kept them awake at night. The pain of this type of headache was most often described as dull, moderating as time went on, and definitely relieved by rest or sleep. The most common associated manifestations occurring during the headaches were anxiety, sweating, depression, and vague symptoms of numbness or vasomotor changes in the extremities. Vague eye symptoms were complained of in a few cases of tension headaches, but when questioned closely the flashes of lights or scotomata of the migraine syndrome were absent.

Most patients presenting the symptom of nervous tension headaches did not have to lose time from their work because of headaches. However, in the majority of cases, patients stated that they did not wish to socialize during their headaches and often preferred to be alone and to rest. Neurological examinations were done on all fifty patients studied for headaches and all were negative except two cases who had previous severe head injuries with resultant neurological changes from those head injuries.

Electroencephalograms were done in twenty-seven cases. Thirteen were abnormal, but in all cases this abnormality could be attributed to previous head injuries or a post-traumatic epileptic state. In no case was it suspected that the patient had either a brain tumor or a severe enough pathological process within the brain to account for headaches.

Summary

The probable mechanism and etiology of tension headaches is discussed. Migraine and tension headaches have been differentiated.

Fifty patients presenting complaints typical of tension headaches, including some with post-traumatic syndromes, were treated with Fiorinal. Forty-eight per cent of the patients obtained good relief; 40 per cent fair relief, and 12 per cent poor relief from their headaches.

Fiorinal appears to be one of the most useful preparations to date for the relief of tension headaches. Easing of the head discomfort was accomplished by one or two tablets without any unpleasant side effects such as drowsiness or gastric upsets. In many cases Fiorinal appeared to temporarily relieve the discomfort from sinus trouble or acute respiratory infections.

Considerable data relative to tension headaches was collected by the use of a special headache chart. Definite emotional factors were present in over 90 per cent of the patients. The two most common locations of pain in our group of tension headaches were the frontal and occipital areas with muscular tension of the neck playing an important role in the pain. The pain in tension headaches was, in most instances, described as variable, dull, or pressure type of discomfort,

moderating as time elapsed and often relieved by rest or sleep.

(Fiorinal used in this study was supplied through the courtesy of Sandoz Chemical Works, Inc.)

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Intensive Insulin Sub-Coma Treatments Combined with Group Therapy in a Mental Hygiene Clinic

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Introduction

Insulin sub-coma, variously known as ambulatory or modified insulin treatment, has now been demonstrated to have a definite place in the armamentarium of the psychiatric hospital, the psychiatric clinic, and in private practice. There is general agreement that insulin in this form has specific physiological and metabolic effects which contribute to the symptomatic improvement of the patient. Since its inception, it has become ever more evident to most workers in this field that insulin sub-coma serves best as an adjunct to psychotherapy.

Sargant and Slater[1] analyzed the published statistics of Teitelbaum, et al.,[2] who compared the results of treatment of psychiatric casualties of combat receiving group therapy, insulin sub-coma, and amytal in separate groups. They concluded that the poor results with insulin sub-coma in this series were due to inadequate treatment. They also noted that patients received an average of twelve insulin sub-coma treatments without any other form of treatment being employed adjunctively. Sargent,[3] who had extensive experience with modified insulin treatment, has reemphasized on several occasions that treatment must be multi-dimensional in approach. Several authors have discussed the length of treatment from the standpoint of the setting in which they functioned, and of the severity of the patient's illness. Polatin, Spotnitz and Weisel[4] concluded from their hospital series of patients, many of whom were schizophrenics and several organics, that patients require treatment for many months. Tomlinson and Ozarin,[5] dealing also with hospital patients, gave treatment up to six months, but terminated after two months if no improvement was noted. Sargant[6] gave treatment for six to eight weeks, the period in which he felt maximum results were obtained for his patients in a hospital treating acute military and civilian casualties. Sadler and Rubin[7] have treated groups of hospitalized psychosomatic patients from six to eight weeks. They describe the psychiatric team as the center of activity of a program using insulin sub-coma as the cohesive factor in forming homogeneous groups of patients. In discussing the insulin sub-shock program in a clinic similar to ours, Nussbaum et al.,[8] make no mention of the time patients spent in treatment. Von Amberg,[9] in private practice, treated his fifty psychoneurotic patients with insulin sub-coma for two-and-one-half weeks.

In our clinic, which constitutes the center of one of the largest conglomerations of veterans' populations, the plan of treatment devised is the result of the observation that patients achieve results in the insulin sub-

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coma program within a period of six weeks. Treatment beyond this point does not offer additional gains, but rather introduces factors which counteract the effectiveness of the program and deprive other patients of treatment space.

Selection of Cases:

In our mental hygiene unit patients are referred by the clinic screening psychiatrist to a panel of staff members who are assigned to the insulin sub-coma program and who meet regularly as a board to evaluate these cases for treatment. Before the patient is presented the intake social worker discusses with him the meaning of his scheduled interview with the board. She also discusses with him reality problems which deal with employment and family management to determine whether there will be any interference with treatment plans. The case is then presented to the board by the social worker. The patient is invited into the meeting room, introduced to all the members and is helped to feel at ease by the informality of the gathering. The questioning of the patient is directed toward eliciting pertinent information relating to indications for insulin sub-coma treatment. In this fashion the patient comes to meet the staff members responsible for his treatment. Should the patient be referred by his individual psychotherapist for adjunctive insulin sub-coma treatment, the latter presents the case and thus becomes part of the Board.

Among the psychoneurotics, complaints and symptoms of anxiety, tension, and its concomitants, loss of weight, loss of appetite, debility, and depression are accepted as criteria of selection. Even in the absence of loss of weight and appetite, patients who present the other symptoms enumerated are selected because they may benefit from the group therapy setting in this program. Patients who have been diagnosed as schizophrenics are selected only if in a state of remission or if contact with reality is maintained to a fair degree. They may also present pan-neurotic symptomatology, including the symptoms mentioned above. It has been our experience that schizophrenics in the more severe stages of the illness fare rather poorly, and we have, therefore, excluded them from our selection of patients. In these cases modified insulin therapy does not halt the progress of pathology and cannot be substituted for electro-convulsive therapy or insulin coma in a hospital setting.

Alcoholics are as a rule unreliable in sustaining the regularity of attendance which is necessary for this course of treatment. Alcoholics accepted into the program are advised against drinking. Some have benefited enormously by this form of treatment, only to relapse following termination.

Many of the patients referred have rejected psychotherapy in the course of the screening process through the clinic. Others have been referred because of the pressure of overwhelming anxiety which required more immediate and intensive help than can be offered through psychotherapy alone. Since in an active mental hygiene clinic there always is an unfortunately long waiting list for psychotherapy, the ready availability of the insulin program gives these patients treatment when it is needed most urgently. Finally, we chose patients who have had previous unsuccessful experiences in psychotherapy or who are currently in therapy though with minimal progress after a reasonably long trial period.

In the series to be discussed here, 40 of the cases are psychoneurotics, and 32 are schizophrenics. In the preparation of these patients for this treatment, the nature and duration of the treatment are described to them by the physician. The patient is told that insulin is only part of the total treatment that he will receive, and the importance of the group therapy sessions is emphasized. In the course of this briefing, the patient's reactions to the various aspects of the treatment process, such as his attitudes to daily attendance, fasting prior to reporting, acceptance of food from the clinic, and last but not least to the prospect of group psychotherapy, are observed and noted carefully. Then he is introduced to the nurse who acquaints him with the physical set-up of the program, the necessary laboratory tests, and the requirements for attendance. This initial contact with the nurse has been found to help the patient bridge the gap into this new experience with a minimal amount of apprehension. The presence of a well-trained psy-

chiatrically oriented nurse has become a *sine qua non* on the insulin ward. A multitude of functions demand of her an ability to adjust to conditions varying from those of the classical nurses' duties to that of group co-therapist.

Treatment Process

Physiological Aspects:

Patients report daily for a period of six weeks. They are placed in bed where the blood pressure and pulse are recorded by the nurse. An initial dose of five units of regular insulin is given by the physician intravenously. The intravenous route is used to hasten the onset of the hypoglycemic state. Dosage is increased by two units daily until a hypoglycemic reaction is obtained with weakness, perspiration, and drowsiness. The average dose is about twenty-five units and the maximum forty units. The hypoglycemic state is terminated after about ninety to one-hundred and five minutes, first with a cup of sweetened orange juice and then with a meal of high carbohydrate content provided by the clinic. Continuous music of a soothing variety on tape recording is played throughout this treatment phase. Since the introduction of this modality into the treatment, restlessness, talkativeness, and otherwise distracting maneuvers on the part of the patient have decreased to a notable extent. The patients are more relaxed and tend to fall asleep sooner. Patients who continue to remain restless and irritable without any abatement, are given about a half of a cup of orange juice to "take the edge off." This is often followed by drowsiness and slumber. Complications of the hypoglycemic state which necessitate termination are myoclonic movements, sensory perceptive disturbances, stupor, and allergic reactions to regular insulin. For the latter, oral administration of antihistaminics is sufficient for the immediate management. Pork insulin is then substituted for regular insulin for subsequent administration.

Psychological Aspects:

After the patients arise from bed they sit around a table where the meal is eaten. At the same time, and for approximately an hour afterward, they engage in discussions led by the group therapist and the nurse. In the sessions we emphasize the factor of interpersonal relationships and their parataxic distortions. While we do not deliberately over-emphasize this approach to the exclusion of others, we feel that these discussions are more meaningful and more rewarding when they stress the patient's characteristic ways of handling his environment and the continuity of these and earlier problem-solving devices.

Frequently we are presented with the problem of the patient who attends the program regularly but makes no active contribution to the group sessions. Formerly we regarded such patients as non-participants. Now, however, we have come to realize that so-called active participation in group psychotherapy need not be verbal, for behavioral changes sometimes occur in silent patients. They often attach great value to the group sessions and request that they be assigned to similar groups when they have been terminated in the program. Recently a patient of this type unwittingly documented our belief in the value of non-verbal participation when he remarked, "since I have been coming here and listening, I'm beginning to see that I cause a lot of the reactions that people have to me. I used to think that people just had it in for me."

Special problems are raised at the end of the treatment period. The patient knows from the beginning that treatment is going to be terminated at the end of six weeks. Hardly has he had time to get acquainted with fellow patients and staff when he has to break off these relationships. As might be expected the situation makes for considerable separation anxiety. This is particularly true in the case of the overly-dependent patient. We deal with this phenomenon as an inevitable and common experience. As a matter of fact, strong transferences are frequent and even are strongly encouraged. In the secure and protective environment of the ward, even suspicious and withdrawn patients may be expected to form surprisingly positive relationships. Despite this "forced feeding" of transference and the anxiety aroused by termination, most patients are able to work through this phase of treatment. One factor facilitating the transition

is the routine which makes the patient leave the program temporarily every day. Another is the fact that the strongest transference and the greatest amount of separation anxiety are found in the "better," less withdrawn patients. It stands to reason that these patients are more likely to find replacements for the people with whom they become involved while in the program. On the other hand, the sicker, less accessible patients are relatively less inclined to form such relationships in the program and hence have less to lose by termination.

We have noticed that suspicious and withdrawn patients often relate to the nurse because of her unique combination of professional and female attributes. It is the nurse who, because of her daily contact with the patient can most advantageously help him to re-establish a feeling of closeness and belonging. It is logical that she would attend the group meetings in order to enable the patient to discuss and clarify these feelings. Her role in the meetings has become an increasingly significant one, so that now she functions as co-therapist in the group.

Results

Treatment results are judged by the extent of symptomatic change during the six weeks period, and the entry of the patient into some form of psychotherapy which is made available in other sections of the clinic. (Table I.) Classified as *markedly improved* are those patients who experience a total amelioration of their presenting symptoms, with disappearance of signs of anxiety, tension, restlessness, and debility. There is a gain in weight, return of appetite, improved sleep, feelings of well-being and good group participation. Of the 72 patients, 14 or 19 percent fall into this group. Three were schizophrenics, and 11 were psychoneurotics. Eight of these patients entered psychotherapy. All of these patients had been employed prior to treatment and returned to their former occupations. An inference could be made to explain why more of these patients did not enter psychotherapy. Assuming that anxiety is a stimulating factor in seeking psychotherapy, removal of the patients' symptoms may result in loss of the incentive to achieve alteration in the dynamic structure of the personality.

TABLE I

	Psychoneurotics	Schizophrenics	Percent
Total Number of Cases	40	32	
Markedly Improved	11	3	19
Moderately Improved	17	19	50
Minimally Improved	10	9	26
No Improvement	2	1	5
Number of Cases which entered psychotherapy	23	13	50

Moderate improvement is evidenced by a gradual but steady lessening of the intensity of the presenting symptoms with the course of progress noticeably taking a favorable turn. Gain in weight and appetite is usually good. In this group the attention was generally focused upon improvements of somatic symptoms and was observed in those patients whose symptoms had been of longer duration, those who had had stronger somatization defenses than the markedly improved group and who were involved in more complex life situations. They had still been making efforts to maintain gainful employment, though irregularly, before they had sought help. There were 36 patients or 50 per cent in this group, 19 being schizophrenic and 17 psychoneurotic.

The *minimally improved* group consisted of 19 patients or 26 per cent. There was some abatement of the symptoms and a small gain in weight. Among them were the somatically fixated, the chronically ill with character disturbances, severe phobics, several alcoholics, and many with intolerable reality problems. The dosage of insulin was difficult to regulate in this group and it was felt by several of the staff that these patients were not cooperating with the regulations about fasting prior to treatments. Group participation was superficial. Seven of these patients accepted appointments for psychotherapy but withheld expressing their feelings fully, adopting "wait and see" attitudes. Nine of these patients were schizophrenic and 10 psychoneurotic.

Three patients, or 5 per cent were *without benefit* entirely. They were disdainful of therapy, showed no appreciable weight changes, and remained aloof from group participation.

The average number of treatments was twenty-nine. The average weight gain was

8.4 lbs. ranging from 2 to 18 lbs. Weight gain was often associated with improved autonomic functioning, though general improvement was not necessarily in direct proportion to the increase in weight.

Two patients had one convulsive seizure each while in treatment. Ordinarily with the onset of mild myclonic jerking, sweetened orange juice can be given orally, which is sufficient to abort a seizure. In these two cases the progression was so rapid that the glucose could not combat the hypoglycemia fast enough. Thereafter dosage was decreased ten to fifteen units and slowly increased one unit at three to four day intervals. No complications followed these seizures.

Three patients returned about ten to fourteen months following termination for repeat courses. All were less ill than when first treated and responded rapidly to the second course. Originally considered in the minimally improved group, these patients now entered treatment with more zest and were more amenable to psychotherapeutic procedure.

Discussion

Several factors have been considered significant in the formulation of the six weeks insulin sub-coma program. The establishment of this arm of the clinic was predicated upon the recognized need to provide a special service to patients in a psychiatric clinic at a time when further functioning without help would be at great risk and strain to the total personality. The purpose of such treatment is to offer a respite from daily tensions and thus head off a progressive breakdown leading to hospitalization. The setting could be compared to that of a modified day hospital, where patients report in the morning and leave late in the day to continue with other relationships at home. However, in our approach, much emphasis is placed on the limiting of the period of attendance to the six weeks of intensive treatment. Foremost is the adequate control of the vicissitudes of fostered dependency resulting from daily attendance, a stay in bed, food provided by the clinic, and the presence of a permissive milieu supplied by a congenial staff. Prior to the changeover to the limited program, patients would remain in treatment for several months and receive as many as one-hundred fifty treatments. These patients tended to lose sight of the purposes of treatment, reported irregularity, formed incohesive groups and developed attitudes of indifference. Some would lose interest and disappear without planning for the future. Others showed a marked reaction of resentment when informed of termination of treatment and this was oft accompanied by a return of the previous symptomatology. The limited period allows for better planning for the patients in handling leaves of absences from jobs, schools, or training situations.

Many of the patients primarily complain of somatic symptoms, and for this and additional reasons have been deemed unsuitable for psychotherapy. A prolonged course of insulin treatment would tend further to fixate symptomatology on a somatized basis and hinder future psychotherapeutic endeavors. Furthermore, as mentioned above, those who have benefited from treatment or have developed attachments to the group, show anxiety as termination approaches. The advantage of contracting with the patients in advance about the length of stay is that requests to prolong treatment can be handled with a minimum of reaction of resentment, which had been encountered previously. In fact, patients themselves usually keep close count of the time remaining. It was noted that a six week period of treatment was inadequate for a few patients. In cases where weight gain achieved a role of importance to the patient, and realistically was part of the patient's health requirements because of an initial debility an extension of the treatment for a week or two was permitted. In the over-all sense, however, repeated courses of treatment of a brief duration, interspersed with periods of activity are more beneficial if considered in the light of the effects of prolonged dependency on the patient's total functioning.

Having thus established the boundaries within which intensive treatment takes place, the dependency needs can now be enlisted to aid in the acceptance of new modes of help. Thus, for example, if patients become more dependent by reporting daily and being fed as part of the treatment, they also become more receptive to the type of set-

ting which offers this gratification. Since this setting also consists of a form of group living, the transition to group therapy can be effectuated by the therapist even with patients who previously had rejected psychotherapy. This skillful maneuver requires a therapist with high human and professional qualifications. Under this regime we have seen the most resistive patient requesting psychotherapy upon termination of insulin treatments. It is our opinion that patients are not "seduced" into therapy in this fashion but rather participate in a new experience in living together with other members of a group.

One of the most satisfying experiences we have had is that of seeing a long-resistant patient leave the program with a determination to undertake psychotherapy or have another try at it, this time a serious one. A typical case of this kind is that of a WW II veteran who complained of G.I. distress for several years, so loud and so long that he had become something of a "cause celebre" in the clinic. While in the program he was helped to see some of the relationships between his symptoms and his characteristic ways of dealing with anger. Following his termination he resumed individual therapy. At last report he had made significant inroads into his illness, with marked improvement in his social life and in his physical symptoms.

Our approach to the optimal functioning of the psychiatric team stresses maximal utilization of individual therapeutic skills. We utilize the unique professional contributions of each discipline. A direct consequence of this philosophy is an immeasurably greater unfolding of personal and professional abilities. Interpersonal relationships among the staff are of tremendous significance in a setting of this type. Our program could hardly have been successful if it were not for the feeling of belonging experienced by each staff member. This feeling is highly contagious, and our patients profit as a result.

Summary and Conclusions

Seventy-two patients were treated with insulin sub-coma dosages for periods lasting six weeks. Thirty-two patients were schizophrenics, forty were psychoneurotics. Group therapy was given concurrently during this time.

Sixty-nine per cent, which include the markedly and moderately improved groups, were distinctly benefitted symptomatically. Fifty per cent were helped to accept some form of psychotherapy on termination of treatment.

Emphasis has been placed on the importance of limiting the period of insulin sub-coma treatments when such treatments become intensive in nature.

Insulin sub-coma has a definite place in a Mental Hygiene Clinic as an adjunct to psychotherapy.

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Metastatic Brain Tumors

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Metastatic carcinoma should always be considered when a patient is first seen with signs of an expanding intracranial lesion. This is especially true of an elderly patient. Knowledge of the tumors which metastasize frequently to the brain is an advantage in locating a primary neoplasm or eliminating the possibility that a primary neoplasm exists.

Reports on the incidence and source of metastatic brain tumors vary from 3 to 40 per cent of all tumors of the nervous system.[1] In fact, I became interested in the subject because I had seen marked variation in the number of metastatic tumors of the brain in four different pathology departments where I had studied. At the Montreal Neurological Institute of McGill University, I saw relatively few metastatic tumors of the brain, whereas, primary tumors were very frequent. Only the autopsies and surgical specimens of neurological and neurosurgical cases were studied in this Institute. However, at the Pathological Institute of the same University, where general autopsies were performed on all types of cases, metastatic brain tumors were frequent.

At the Veteran's Administration Center in Los Angeles, where over 900 autopsies are performed each year, the autopsy per cent is high (79%) and the brain is studied in almost every case, I was amazed at the high incidence of metastatic tumors of the brain. In 1953, I reviewed 3,946 necropsies at this center, for the five year period 1948-1952 inclusive, and reported 167 metastatic tumors of the brain (in 1,498 cancer cases) and only 99 cases of primary intracranial tumors.[2] These were all adult male veterans, and the average age was 57 years, making this a select study of adult males.

When I returned to the University of Texas Medical Branch in Galveston, I decided to repeat this study because this university consists of a group of hospitals which has, for many years, functioned as a large general hospital and necropsy records are available since 1892. While this study was going on, several interesting reports of similar nature appeared in the literature[7,8,9] and it became possible to compare our findings with those of similar institutions.

The purpose of this paper, therefore, is as follows: (1) to report the incidence, primary sources, and anatomical locations of metastatic tumors in 9,700 necropsies at the University of Texas Medical Branch, (2) to compare the findings with those of other hospitals, (3) to consider the factors responsible for statistical variations, (4) to draw some conclusions concerning the most frequent primary sources and the probable routes of metastasis.

Factors Causing Statistical Variations

From October, 1892 to August, 1954, there are records of 9,720 necropsies at the University of Texas Medical Branch in Galveston, Texas. A study of these records revealed that 1,441 of the cases had one or more malignant neoplasm contributing to death. The findings in the brain were reviewed in all of these cases. This immediately brought to my attention one of the major reasons why figures on the incidence of metastatic brain tumors vary so widely. Of the 1,441 cancer cases, the brain was examined in only 710 cases, approximately one-half. I am sure that this is no reflection on the University of Texas. It is common knowledge that the brain is not removed in every necropsy for a variety of reasons. The usual reasons for failure to examine the brain are: (a) limitations of the necropsy permit, (b) objections of the mortician, and (c) limitation of time and facilities, especially in those cases where the cause of death is obvious from the general findings. Much valuable information is lost by limitation of

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the necropsy. During the past year, with the splendid cooperation of all concerned, the brain has been examined in 83% of the necropsies, that is, whenever the permit allowed this examination.

A second factor that influences the reported incidence of metastatic brain tumors is the necropsy percentage itself. In this series of cases, the necropsy percentage varied from 14% in the early years of the Medical School to a high of 86% in 1947. The overall average for the years in which percentages were accurately calculated was about 60%.

A third factor, which defies computation, is the fact that many of the cases with malignant neoplasm leave the hospital when they have received the maximum benefits of in-patient care, and eventually succumb at home. Necropsy is not performed on most of these cases.

A fourth factor is the nature of the hospital or clinic where the study is made and the methods used in reporting results. In highly specialized neurosurgical clinics, the incidence of metastatic brain tumors is low. Cushing[12] found only 3.2% metastatic tumors in his series of 2,000 cases of verified intracranial tumors. He stresses the fact that his cases were highly selective. In a general hospital or Veteran's hospital, the percentage is high. Courville[3] found 221 cases (24.7%) in a series of 847 intracranial tumors at the Los Angeles County Hospital. The author[2] found 62% in a series of 266 intracranial tumors at the Veteran's Administration Center in Los Angeles. The percentage was high at the Veteran's hospital because the brain was examined in almost every case, and many cases of malignant disease were referred to this hospital. Many of the objections to brain removal are overcome in the Veteran's hospitals by the fact that embalming is done before the necropsy. Removal of the brain does not, therefore, interfere with the usual embalming procedures.

A fifth factor is the method of reporting results. Some reports simply review the number and types of tumors which were found in a series of brains studied without reference to the autopsy percentage, how many times the brain was actually examined or how many cancer cases actually came to autopsy.

Other important factors are as follows: Certain types of cancer may be increasing in frequency, notably bronchogenic carcinoma.[7] Cancer cases as a whole are increasing in frequency as a cause of death.[6] Diagnostic and neurosurgical procedures have improved and more cases may now be seen in hospitals.

Undoubtedly there are other factors, but these seem to be the most important.

TABLE I—*Chart Showing Number of Cancer Cases and Primary Sources of Mestastatic Brain Tumors in 9,720 Necropsies at the University of Texas Medical Branch in Galveston from 1892 to 1954.*

PRIMARY SITE	Total number of cases	Brain examined	Metatatic to brain	Average age in years
Melanomas	17	14	8	57.5
Lip	4	1	0	63.0
Salivary glands	5	2	0	66.4
Mouth & gingiva	3	2	0	55.0
Tongue	8	3	0	59.8
Nasal sinuses & nasopharynx	8	6	2	41.2
Tonsil	3	2	0	53.9
Pharynx	3	0	0	52.3
Larynx & hypopharynx	17	5	0	58.9
Thyroid	9	*	1	54.3
Trachea	2	2	0	57.0
Bronchus & lung	133	77	24	57.8
Mediastinum & pleura	6	2	0	46.5
Esophagus	50	19	1	59.2
Stomach	158	46	2	56.9
Small intestine	3	1	0	49.0
Large intestine	78	31	0	59.4
Liver	43	14	0	52.6
Gallbladder & bile ducts	33	11	0	62.3
Pancreas	90	32	2	59.7
Adrenal	18	12	5	26.4
Kidney	29	12	1	42.8
Renal pelvis & ureters	2	1	0	68.5
Bladder & urethra	35	14	0	64.1
Prostrate	89	46	0	69.9
Testis & seminal vesicles	4	1	1	57.0
Penis	4	1	0	59.0
Ovary	15	4	1	50.1
Uterus	24	8	2	49.3
Cervix	52	10	1	48.6
Vagina & vulva	2	0	0	77.0
Breast	41	21	6	49.6
Bone & joints	21	12	1	43.3
Sarcomas of soft parts	23	6	1	45.8
Lymphomas & leukemias	181	94	17	38.4
Brain & coverings	175	175		38.7
Spinal cord & coverings	5	5	0	28.6
Uncertain primary	48	12	3	49.2
TOTAL	1441	710	79	Average 53.4

(Note: Of the 710 brains examined 175 had a primary intracranial tumor, 79 contained metastatic tumor and 456 showed no evidence of metastasis.)

The Necropsy Findings

Of the 710 brains which were examined in the 1,441 cases with a malignant neoplasm in 9,720 consecutive necropsies from 1892 to 1954, 79 contained metastatic tumor (Table I). Carcinomas of the skin are excluded from the 1,441 tumor cases, since most of them were localized lesions and not every suspicious skin lesion was biopsied. Pituitary adenomas are not included since most of them were incidental findings, or showed no evidence of invasion beyond the sella turcica. Melanomas showing metastasis, carcinomas of the lip and anus are included. Lymphomas and leukemias are included as a group since they are considered to be related neoplasms. Only those cases showing definite invasion of brain parenchyma or leptomeninges are included.

Metastases to the skull or dura alone are not included in the 79 cases unless there was definite invasion of the brain substance as well. Metastases to the skull and dura usually produced no neurological signs, but an occasional case produced a large mass which depressed the underlying brain or invaded it. In some cases the metastasis grossly resembled a meningioma. The spinal cord was removed in so few cases that metastases to this part are not included. Metastases to the pituitary alone are not included. Direct invasion of the brain by carcinomas of adjacent structures are included.

The primary sources of metastatic tumors were as follows: melanomas, 8 cases; nasal sinus and nasopharynx, 2 cases; thyroid, 1 case; bronchus and lung, 24 cases; esophagus, 1 case; stomach, 2 cases; pancreas, 2 cases; adrenal, 5 cases; kidney, 1 case; testis, 1 case; ovary, 1 case; uterus, 2 cases; cervix, 1 case; breast, 6 cases; bone, 1 case; sarcoma of soft parts, 1 case; lymphomas and leukemias, 17 cases; uncertain primary, 3 cases.

Among the adult men, bronchogenic carcinoma was, by far, the most common primary source. Among the adult women, carcinoma of the breast was the most common source. Among the children, neuroblastomas of the adrenal, lymphomas and leukemias were the most common sources.

Multiple metastases in the brain were more common than single nodules. Single metastases were found in 18 cases, multiple nodules in 57 cases, and direct invasion from adjacent structures in 4 cases. Thus, single metastases were found in only one-fourth of the cases and the metastases were multiple in approximately three-fourths of the cases.

Metastases were most frequent in the cerebral hemispheres than in the cerebellum. In the cases with a single metastatic focus, the cerebrum was the site in 12 cases, and the cerebellum in 6 cases. The single metastases of the cerebrum occurred in the right hemisphere 7 times, left hemisphere 4 times, and the side was not stated in 1 case. This agrees with most studies that show no particular preference for either hemisphere.[2,3,4] The lobes which were chiefly involved were as follows for the single metastases: temporal, 3 cases; parietal, 4 cases; frontal, 2 cases; occipital, 1 case; basal ganglia, 1 case; insular region, 1 case; cerebellum, 6 cases.

The various locations indicate that metastatic carcinoma may occur anywhere in the brain, but the regions supplied by terminal branches of the middle cerebral artery seem to be the favorite location. This, of course, covers a wide area of the brain from frontal to occipital lobes, but the posterior regions of the brain, especially the temporo-parietal regions seem to be most common in this series of necropsies.

Diffuse carcinomatosis of the leptomeninges sometimes occurs without metastases elsewhere in the brain. This was found in 11 cases. This condition has been seen by the author three times in the past year and the clinical diagnosis was correctly made in two of the cases. These patients show diffuse signs resembling meningo-encephalitis with or without involvement of various cranial nerves. In some cases, the malignant cells can be identified in the spinal fluid. In the 11 cases of this series, the primary tumors which produced diffuse carcinomatosis of the leptomeninges were as follows: melanoma, 3 cases; thyroid, 1 case; bronchus, 1 case; neuroblastoma of adrenal, 2 cases; lymphomas and leukemia, 4 cases.

Cases of diffuse carcinomatosis of the leptomeninges have been reported as complications of various primary neoplasms.[3] Melanomas, lymphomas, carcinoma of the lung, breast and thyroid are the most common

sources in my experience. Courville[3] states that meningeal localization occurs from carcinoma of the stomach as well and my be a characteristic of this type. I have not yet seen a case of this type from carcinoma of the stomach. In fact, carcinoma of the stomach rarely metastasizes to the brain in my experience. In 108 cases with carcinoma of the stomach, seen at the Veteran's Administration Center in Los Angeles, metastases were found in the brain only 3 times. In this series of necropsies there were 158 cases of carcinoma of the stomach. The brain was examined in 46 of the cases and metastases were found in only two cases. None of the cases showed diffuse spread in the leptomeninges.

The lymphomas and leukemias are grouped as related neoplasms in this study. Both groups may produce cellular infiltrations of the brain similar to other neoplasms. The leukemias more often produce anoxic changes of the vessel walls, probably due to anemia and packing of the vessels with leukemic cells, which result in focal or massive hemorrhages. In some cases the leukemic cells fill the small vessels and result in infarctions which may be anemic or hemorrhagic, depending on collateral circulation and completeness of the occlusion by leukemic cells. In other cases there is a remarkable degree of infiltration of the brain substance by the leukemic cells without the presence of significant hemorrhage. The leptomeninges and nerve roots may be extensively infiltrated and exhibit bizarre neurological signs. The spinal fluid in these cases may show only a slight increase in protein with little or no increase in cells if the infiltrations are localized. In this study, four cases of lymphoma or leukemia were found with diffuse spread in the leptomeninges, whereas most of the cases produced focal hemorrhages or infarctions. Of these four cases, 2 were myelogenous leukemia, 1 lymphocytic leukemia, and 1 lymphosarcoma.

Routes of Metastasis:

From the anatomical locations and types of metastatic carcinoma which were found in the brain, the evidence is overwhelming that these metastases arrive through the arterial blood stream. Invasion of the brain by carcinomas of adjacent structures (such as nasal sinuses) or secondary invasion of the brain by metastatic carcinoma to the dura or skull are much less common than arterial metastases to the brain. Metastasis to the brain along perineurial lymphatics is uncommon.

The most common route of metastasis to the brain seems to be by invasion of a pulmonary vein. This explains why carcinoma of the lung is the most common primary source of metastatic brain tumors. Once the tumor has invaded a pulmonary vein, the tumor cells are carried through the left atrium, left ventricle and thence out the aorta, through the carotid artery to lodge in the small branches of a cerebral artery, most often a branch of the middle cerebral artery. Carcinomas of the breast are common sources of brain metastasis, probably because they metastasize frequently to the lung. Once a metastasis is established in the lung it may erode a pulmonary vein and disseminate in the same manner as a primary lung tumor.

Carcinomas of the stomach and intestines seldom metastasize to the brain, probably because of the tendency of these tumors to first invade the regional lymphatics or portal venous system and lodge in the liver or lymph nodes. In order to reach the brain, metastases must reimplant in the lung, erode into a pulmonary vein and thus gain access to the arterial circulation.

Metastases to the brain, in the absence of visible lung metastases, are difficult to explain (so-called paradoxical metastases). Six possibilities exist, but all lack decisive proof. The most likely possibility is that tumor cells pass through capillaries of the lung in some cases. There is little direct evidence to suggest that this is possible, but indirect evidence is rather convincing.[14,15] That is, experimental injection of particles of large size have been passed through the capillaries of the lung and some clinical cases of fat embolism of the brain following fractures can only be explained in this way. These particles are as large as clusters of tumor cells.

The other five possibilities seem less likely. These are: (a) tumor cells may reach the arterial circulation by passing from right at-

rium to left atrium through a patent foramen ovale, but cases of paradoxical embolism have been seen in which the foramen ovale was closed, (b) tumor cells may implant in the myocardium and secondarily erode into the left atrium or left ventricle, but this must be extremely rare, and I have never seen such a case, (c) tumor cells may bypass the lung by passing in retrograde fashion up the vertebral venous system of Batson,[5] but metastases to the brain are seldom found in the vicinity of this venous system. This route of metastasis has been highly overrated in my opinion. (d) Tumor metastases may actually lodge in the lung and be too small to be seen on gross examination. (These metastases may be missed in sampling the lung. This is very likely the explanation in some cases as it is certainly impractical to serial section both lungs to prove the point), (e) a few tumors may invade along perineurial lymphatics, gain access to the spinal fluid and implant in the subarachnoid or subdural spaces (some of the tumors of the spinal cord seem to have traveled by this rouse).

Conclusion and Comparison With Other Reports

Cases of metastatic carcinoma of the brain seem to be observed with increasing frequency. Over half of the cases of metastatic brain tumors in this series have been recorded in the past five years. This may be due to the general increase of cancer as a whole,[6] improved diagnoses and treatment or to a relative increase in the incidence of carcinoma of the lung.[7] Whatever the cause, these cases seem to be more frequent and we

TABLE II—*Chart Showing Comparison of the Findings in This Study With Those of Eight Other Similar Studies.*

	University of Texas, Galveston (Earle)	Veterans' Administration Center (Men only) (Earle)[2]	University of Melbourne (Willis)[13]	University of Minnesota (Baker)[4]	Mayo Clinic (Kiefer)[10]	Los Angeles County Hospital (Courville)[3]	Henry Ford Hospital, Detroit (Knights)[7]	Serafimerlasarettet Stockholm, Sweden (Stortebecker)[8]	Montefiori Hospital New York Lesse & Netsky[9]
Bronchus & Lung	24	96	9	24	34	86	25	25	50
Breast	6	1	7	24	11	21	19	11	71
Melanomas (including eye)	8	12	2	11(?)	9	25	6	12	3
Lymphomas & leukemias	17	5			2		13		20
Mouth & pharynx				1			2		
Nasal sinus & nasopharynx	2	6		1			1	2	4
Thyroid	1	1		2				2	6
Tonsil		1		1					
Esophagus	1		2	1			1	3	
Stomach	2	3	1	4	[illegible]	GI tract incl. pancreas & liver—22	3	5	[illegible]
Liver, gallbladder & bile ducts		1		1	1				2
Pancreas	2	3	1	4	1		3	1	
Intestines	0	11	1	8	14		4	6	7
Adrenal	5	3		6					
Kidney	1	8	3	9	10		3	32	10
Prostate		2		1	2		3		5
Testis	1	8		3			1	3	
Bladder		4		2			1		
Ovary	1			1	2		1	2	
Uterus	2			5			1	2	3
Cervix	1								
Bone	1	2		1			4	1	5
Sarcomas (other than above)	1		1		2	10	6		3
Other sites			2		2	42	4		
Uncertain primary	3					20	1	51	
TOTAL	79	167	29	114	100	256	102	158	193

Male genital tract—4
Female genital tract—8
Urinary tract—6
Endocrine glands—7
Skin & app.—5

*Although not definitely stated, the discussion indicates that most of the 9 tumors of skin and 2 of eye reported by Baker were melanoma.

should be aware of the tumors which most frequently produce metastases to brain while realizing that almost any cancer may occasionally do so.

Although this study, and others, indicate that only about one-fourth of the metastases to the brain are single at the time of necropsy, the neurosurgeon should not be discouraged from attacking these lesions since the palliative effects may be surprisingly good.[8]

This study is compared with reports of eight other hospitals and clinics (Table 2). All of these reports have appeared since 1942. The subject of metastatic brain tumors prior to 1942 is well reviewed by Baker.[4]

Many of the factors causing differences in these reports have already been discussed and some others must be mentioned. Lesse & Netsky,[9] do not include children in their series and do not include cases of uncertain primary site. They state that many cases of carcinoma of the breast are admitted to their hospital and this may account for their high incidence of this type. In Baker's[4] series only 92 of 144 reported metastases were studied pathologically, and the exact number of melanomas is not given, but it is assumed from the discussion that most of the 9 skin tumors, and 2 eye tumors were melanomas. The figures from the Veteran's Administration Center[2] are compared, but it must be remembered that these were all adult men. Almost all of the cases of carcinoma of the breast in all of the studies were adult women. Most of the cases of carcinoma of the lung in all of the studies were adult men. (In the University of Texas series, bronchogenic carcinoma was found in 122 men, 11 women and no children, while carcinoma of the breast was found in 39 adult women, 1 man and one child.) In the University of Texas series, and some of the others, men outnumber women as a whole. In this study of 1,441 cancer cases, there were 949 adult men, 390 adult women, and 102 children (under 16 years).

Despite the many factors leading to discrepancies, the various reports show some remarkable similarities. Carcinoma of the lung is the most common primary source of brain metastases in adult men, and carcinoma of the breast is most common in adult women (Table 2). The children are not compared in most reports and few in others, but the University of Texas series showed neuroblastomas of the adrenal and leukemias to be most common primary source of metastases in this group.

Metastases to the brain from carcinoma of the stomach are rare in all of the reports despite the high incidence of this type of cancer. Carcinoma of the large intestine is infrequently the primary source of brain metastases, but seems to be slightly more common than carcinoma of the stomach, esophagus, small intestine, liver, gallbladder or pancreas (Table 2).

Carcinoma of the prostate is a common malignant neoplasm of elderly men, but metastases to the brain are infrequent. In my experience, these metastases usually involve the cranium of dura first, and secondarily invade the underlying brain.

Stortebecker (Table 2) had an unusual number of metastases from carcinoma of the kidney. This was the most common primary site in his series, but he states that among his 51 cases of uncertain primary site (only surgical specimens were available in these cases) that some may have been from the lung.

Melanomas are not as common as some neoplasms, but they metastasize frequently to brain. Over half of the melanomas in this series showed brain metastases.

As a conclusion it should be stated that metastatic tumors of the brain are much more frequent than most textbooks and reports have indicated previously. In a recent book the following statement is made, "Neoplasms metastatic to the brain comprise 3 to 5 per cent of all brain tumors. . ."[11] This figure is far too low and shows that Cushing's figures, although explained by him as being low due to his type of specialized clinic, continue to be quoted without qualification. At the Veteran's Administration Center in Los Angeles, metastatic tumors were seen more frequently than primary intracranial tumors. At the University of Texas 175 primary intracranial tumors were seen and only 79 metastatic brain tumors; *but the brain was examined in only half of the cases who died with a malignant neoplasm.* It is highly

probable that many more were not found since autopsies on neurosurgical cases were over 90% while the general autopsy percentage was about 60%. Furthermore, a large number of cancer cases left the hospital and succumbed at home. No autopsy was performed in most of these cases. When all of these factors are considered, it seems reasonable to assume that metastatic tumors of the brain are as common as primary intracranial tumors, if not more so.

Summary

The records of 9,720 necropsies at the University of Texas Medical Branch, Galveston, Texas, from 1892 to 1954, revealed 1,441 cases of malignant neoplasm. These records were studied and revealed that the brain was examined in 710 cases and metastases were found in 79 brains. The factors causing statistical variations on the incidence and type of metastatic brain tumors are discussed. When all of the factors are considered, it seems likely that metastatic tumors of the brain are as common as primary tumors, if not more so.

The primary sources of the metastatic tumors were as follows: melanomas, 8 cases; nasal sinuses and naopharynx, 2; thyroid, 1; bronchus and lung, 24; esophagus, 1; stomach, 2; pancreas, 2; adrenal, 5; kidney, 1; testis, 1; ovary, 1; uterus, 2; cervix, 1; breast, 6; bone, 1; sarcoma of soft parts, 1; lymphomas and leukemias, 17; uncertain primary, 3 cases.

Multiple metastases were found in 57 cases and single metastases were found in only 18 cases. The cerebral hemispheres were the most common sites of metatases.

Diffuse carcinomatosis of the leptomeninges, lymphomas and leukemias are discussed.

The findings indicate that the arterial circulation is the most common route of metastasis. The other possible routes are considered.

The results of this study are compared with similar reports from eight other hospitals.

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Experimental Use of Pregnenolone Methyl Ether In Treating Psychiatric Symptoms

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In recent years there has been mounting interest in the search for more effective pharmacological agents to modify psychiatric symptoms. These symptoms assume many forms, and out of the medical search for means to eliminate them has come an overwhelming variety of preparations and infinite confusion regarding their effectiveness.

Many factors contribute to this confusion. Although psychiatric symptoms involve changes in physiological function, the exact nature of these changes is seldom completely understood, and the origin of these changes often becomes a matter for theoretical debate among those who know the most about them, as well as among those who know the least. Drug houses which sincerely try to supply materials to fill medical needs are often carried away with the enthusiasm of early glowing reports. Physicians, who are trained to be skeptical, may lose their skepticism in the rising hope of finding more effective ways to treat their patients.

And then the reaction sets in. The early glowing reports are not verified by other workers. Factors at first not considered are found to be very important. Disappointment prevails. Finally the medicine is coldly scrutinized and fitted into the role where it performs most effectively.

The substances known as steroids have been particularly difficult to evaluate. Many volumes have been written about these compounds, and still their function is poorly understood. Their effect on the physiology of the nervous system is especially controversial.

The estrogens seem to have a profound effect in some cases and none in others that appear quite similar. Testosterone also produces inconsistent results. Undesirable side effects may limit clinical usefulness.

In the search for remedies for arthritis, Cortisone and related compounds were found to produce a marked feeling of relief before objective changes could be observed.

Dr. Max Huffman, of the Oklahoma Medical Research Foundation, chose Pregnenolone Methyl Ether (PME) as the most promising of one series of steroids investigated over three years ago, for use in the treatment of arthritis and hypersensitivity diseases. PME showed no demonstrable toxic properties and no androgenic or estrogenic effect in extensive tests on rats. Patients receiving PME as treatment for arthritis described a feeling of well-being, but no marked objective decrease was seen in the arthritic process. After this reasonably consistent subjective improvement was noted even in cases previously non-responsive to other preparations, it was suggested that a trial be made in treating psychiatric symptoms, where a reduction in anxiety is often a vital matter difficult to obtain.

Since this steroid is almost insoluble in water even at body temperature, it has been necessary to give it orally in a digestible oil solution, of 25 Mgm/cc strength. Because the oil carrier causes digestive disturbance in large doses, it has not been practical to push the daily dose beyond a level of 1000 Mgm, but since therapeutic effects in most instances have been obtained at daily divided dosage levels of 150 to 500 Mgm, the carrier has been a practical one.

The first clinical evaluations of the effects of PME on psychiatric symptoms were carried out under the direction of Dr. Coyne H. Campbell, and this report is formulated from the work done with private patients treated at the Coyne Campbell Sanitarium. These clinical trials have extended over a period of almost two years.

It was decided early that no detailed statistical data would be expected from the first stage of clinical observation. From this first series of 150 patients, the hypothetical effects of PME were formulated, and more

detailed work is now being carried out to test these hypotheses.

No significant change was noted in disorders affecting content of thought. Only a few attempts were made to push the dosage to a high level in severe psychotics, but no demonstrable change was noted in these.

The only frequent alteration seen in the patients taking PME was a decrease in irritability and anxiety, which change appeared to occur within a limit characteristic of each patient. Pushing the dosage level higher produced no great change after this limit of improvement was reached. A healthy sleep pattern was often restored along with the diminished anxiety.

The only two major groups of patients who seemed to be very favorably affected were among the involutional patients with anxiety and depression, and among the psychoneurotic patients who had become stable with the passage of time, but remained uncomfortable because of their neurosis.

A sincere attempt was made to reduce or eliminate the effect of suggestion on these patients; and it was the clinical opinion of the workers on this project that the preparation used was pharmacologically active, and its effects definite enough to warrant continued study.

It is important that no disturbance of judgment or concentration was noted in patients who improved on PME. No sedative or cortical suppressive effect was seen. The stimulating effect of drugs such as amphetamine was not observed with PME, and there were no withdrawal symptoms. The only side effects noted were an occasional mild rash, which never became a great problem, and which may have been due to the oil carrier. Occasionally a mild nausea would occur when the dose was large and given on an empty stomach. The only suggestions of hormonal action were seen in women, where an occasional patient would complain of weight gain and difficulty in losing weight, and a few would mention an increase in menstrual irregularity. In pre-menstrual tension there was a marked improvement, with reduction of irritability and emotional instability.

At the present time Merck & Company is supplying this steroid for limited experimental study in compliance with FDA regulations.

In Oklahoma City further study is being made of the effects of PME in involutional patients. Dr. Huffman is still searching for a steroid that is more efficient and consistent in its effects. In Galveston, the effects of PME in adrenalectomized schizophrenics are being investigated. In other centers, the possibilities of vascular and skin temperature changes are being considered.

Perhaps Pregnenolone Methyl Ether may not appear very dramatic in the flush of enthusiasm over the effects of Chlorpromazine and the preparations from the rauwolfia plant, but this paper should remind us that in the field of the steroids we may yet find more useful tools to help us in the treatment of our patients.

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Book Reviews

ANATOMY REGIONAL AND APPLIED by R. J. Last, M.B., B.S., F.R.C.S., Little Brown & Company, 665 p., 309 illustrations, $10.00 (1954).

The book has been arranged sectionally into seven subdivisions.

The first section discusses in a capable manner, the embryological, anatomical and where deemed essential to easier understanding, the practical physiology of tissues and structures. The nervous system is detailed as to general principles of innervation, peripheral distribution, topography of dermatomes, myotomes and autonomic system.

The ensuing sections through the book are taken up by regions, each of which follows a descriptive format based upon a structural and operational plan, with detailed anatomic and functional description of the specific neurological architecture of the bodily region under consideration.

One eighth of the book contains an excellent section on the central nervous system which is informatively generous with neuro—applied—and topographical anatomy. This section is concluded with a descriptive summary of the development of the nervous system from its ectodermal origin.

Much information of clinical value may be found under each of the sections, and the volume is profusely illustrated by drawings and photographs, a number of which are in color.

The book appears to have been planned on the principle of relationship of structural to functional aspects of anatomy; and liberal clinical references thereto may be found throughout its pages.

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A DICTIONARY OF PASTORAL PSYCHOLOGY by Vergilius Ferm and others. Philosophical Library, New York, pp. 333, $6.00.

This volume addressed to ministers is published in order to present to men of the cloth disciplined information concerning a highly complex field. It comments upon and sometimes defines the various psychological problems which the clergyman encounters in his pastorate. Though entitled PASTORAL PSYCHOLOGY, the author indicates that there is no psychology which is purely pastoral but rather the descriptive adjective is used to cover the application of the general principles of human psychology in the areas in which the minister works.

There are definitions of terms and concepts, discussions brief and at length, descriptions, comments —most of them objective, all of them sincere—of numerous things from Ability to Zenophobia. Some of the longer discussions contain examples and case descriptions and in these the author is assisted by six special contributors, four ministers, one physician and a rabbi. There are suggestions for the Protestant chaplain, suggestions for the preparation of sermons, a few pages given to the discussion of teen agers, and even a line entitled "bad temper—see complexes." All in all it covers a wide range of definitions and accomplishes the purpose for which it was intended—namely to be a dictionary of the terms used in a special discipline.

One dislikes quibbling over little things but there is a question in this reviewer's mind regarding the diagnosis and treatment of "Climacterium Virile" in the man mentioned on page 192, for instance. This is a minor point, however, for the clergyman is not called upon to make a diagnosis and when he does he courts trouble, so we shall pursue this point no further. The volume will be a handy reference for Protestant clergymen.

Francis J. Braceland, M.D.

BOOKS RECEIVED

For readers' attention, books received are descriptively identified. Selected reviews appear in BOOK REVIEW section as space and interest permit.

INTRODUCTION TO PSYCHIATRY. By O. Spurgeon English, M.D., Professor and Chairman, Department of Psychiatry, Temple University School and Hospital, Philadelphia, and Stuart M. Finch, M.D., Assistant Professor of Psychiatry, Temple University School and Hospital, Philadelphia. $7.00, Cloth, Pp. 621, W. W. Norton & Co., Inc., 101 Fifth Avenue, New York, 1954.

PSYCHOANALYSIS AND THE EDUCATION OF THE CHILD. By Gerald H. J. Pearson, M.D., Dean, Institute for the Philadelphia Association for Psychoanalysis. Cloth. $5.00. PP. 357. W. W. Norton & Co., Inc., 101 Fifth Avenue, New York, 1954.

THE PSYCHIATRIC INTERVIEW. By Harry Stack Sullivan, M.D., Cloth. $4.50. Pp. 246. W. W. Norton & Co., Inc., 101 Fifth Avenue, New York, 1954.

HANDBOOK FOR MENTAL NURSES. By Royal Medico-Psychological Association. Eighth Edition. Cloth. $5.00. Pp. 476. The Williams & Wilkins Co. Mt. Royal and Guilford Avenues, Baltimore 2, Md., 1954. Bailliere, Tindall & Cox, 7-8 Henrietta Street, London, 1954.

LEGAL MEDICINE. Edited by R. B. H. Gradwohl, M.D., Sc.D., Director, Police Laboratory, St. Louis Police Department; Pathologist to Christian Hospital. Cloth. $20.00. Pp. 1093, with 222 illustrations. C. V. Mosby Co., 2307 Washington Blvd., St. Louis, 1954.

FUNDAMENTALS OF PSYCHOANALYTIC TECHNIQUE. By Trygve Braatoy, M.D., Cloth. $6.00. Pp. 404. John Wiley & Sons, Inc., 440 Fourth Avenue, New York, 1954.

THE STUDY OF THE BRAIN. By Hyman S. Rubinstein, M.D., Ph.D., Attending Physician (Neurology and Psychiatry) Aberdeen Proving Ground Army Hospital. Cloth. $9.50. Pp. 209, with 93 figures and 43 plates. Grune & Stratton, Inc., 381 Fourth Avenue, New York, 1953.

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